pending upon the result of the microscopic examination, should be skin grafting; further excision and grafting, or amputation.

5. As the history of almost all of these cases of severe and chronic dermatitis dates back to early exposures, with the protection which our present knowledge demands, it is to be hoped that the number of victims of too enthusiastic work in an untried field, will steadily diminish.

6. In the meantime, I have no hesitation in recommending the *early excision* of all *persistent X-ray ulcerations,* in order that subsequent malignant degeneration may be prevented.

PATHOLOGICAL REPORT.

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The pathological report which follows is based upon the study of forty-three microscopic slides presented by Dr. Porter. The sections were already stained, for the most part by the hæmatoxylin-eosin, iron-hæmatoxylin and methylin blue-eosin methods. It is to be regretted that no fresh material was at hand for the special staining of connective tissue and elastic fibrils. The first sections date from July 17, 1902, and were as follows:

1. *Finger of Right Hand.*—Keratosis moderate. Rete somewhat hypertrophic and shows an increased tendency toward downward proliferation. Corium normal and presents no marked signs of inflammation. The deeper horizontal vessels, however, exhibit serious changes. In places veins appear displaying extraordinary mural thickening. No interior alterations are present beyond a slight enlargement of the cells but the outer coats are greatly hypertrophied. Here and there arteries are totally obliterated by endothelial overgrowth.

2. *An Ulcerated Area.*—The rete, where existent, is totally abnormal. The stratum corneum consists of a few lamellæ of non-nucleated cells. The stratum granulosum is absent. The stratum spinosum is made up of greatly dilated cells, the extra-nuclear protoplasm being much rarified and the nuclei shrunken, murally placed, or entirely gone. The palisade layer, however, shows comparatively normal elements. Here and there are masses of red blood cells, suggesting golden pigment granules and filling the whole depth of the rete.

As the ulcer is approached the spinous cells show more distinct configuration but are horizontally elongated and interspersed with erythrocytes.

Corium.—Below this abnormal epidermis there are occasional masses of plasma cells accompanied by a rare mast cell. The papillary and subpapillary vessels are dilated and many are clogged with red cells. Larger deeper vessels are choked with endarterial masses of nucleated cells. This condition is extraordinarily abundant—the lumen of some vessels of great size being entirely obliterated.

Invading the entire corium are polymorphous masses of epithelial cells ranging from small strings to great clumps with many smaller epithelial pearls. The epitheliomatous masses are outlined by a limiting band of deeply staining cells. Within these peripheral bands the cells are often oval and greatly enlarged with correspondingly hypertrophic nuclei containing one or two nucleoli. Some of the cells are really enormous (fusion?) while around them appear epithelial cells whose limiting membranes are indistinct and whose nuclei have disappeared. The epithelial pearls are large, some of them consisting of a nucleated centre surrounded by 15 to 20 concentric hyaline rings.

Mitoses are rare and between these epithelial masses are numerous cells.

3. *From a Finger.*—For the most part the epidermis is normal although the rete is somewhat hyperplastic. In one place, percontra, the spinous layer has receded to three or four layers of somewhat amorphous cells illy defined from the underlying corium and exhibiting deeper proliferation suggestive of epithelioma while above a nucleated crust appears.

The corium shows in the middle and lower layers a few highly dilated lymph spaces and some moderately enlarged blood vessels surrounded by dense plasmomata with an occasional mast cell; while still deeper are seen blood vessels presenting an obliterating endothelial change, and again others with persistent but distorted lumen and thickened walls surrounded by dense envelopes of connective tissue.

4. *From a Finger.*—Within the lobules of epithelioma are many large oval and round, swollen, pale-staining cells—some of great size. The progressive steps towards the formation of pearls can be demonstrated easily. Again mitoses are rare.

5. *Finger of Left Hand* (see photograph 3).—*Rete.*—Where the epidermis is intact there is a marked parakeratosis and acanthosis. The horny layer is decidedly thickened and nuclei persist; the stratum granulosum is absent; the upper layers of spinous cells are flattened and elongated and more or less devoid of nuclei and the whole rete somewhat hyperplastic. In several places the epidermic origin of the epithelioma is plainly manifest and broad masses of tumor cells are seen in direct continuation with the overlying rete.

Throughout the depth of the corium are seen lobules and whorls of epitheliomatous cells between which the collagenous bundles form a delicate meshwork in which are lodged masses of mononuclear cells—for the most part plasma cells—and very numerous, small, dilated vessels. Before any degenerative alterations have developed the cells of the outer layers of the lobules retain their prickles undiminished. With the onset of degeneration, however, we note a disappearance of these spongioplastic prolongations and a concentric arrangement of the cells. Within these onion-like lamellæ the cells assume a roundish configuration with occasional great perinuclear halos while in the centre of the mass appears a basic-staining substance reminiscent of keratin. These conditions well illustrate the epidermic derivation of the tumor masses by their analogy to the progressive cornification of the normal epidermis.

In other parts of the section the epidermis shows less keratosis while the rete produces long finger-like projections into the corium. Finally, in still other areas, there is ulceration. The lowermost layers of the rete alone persist as round or oval, swollen cells; while again all signs of the epidermis are wanting and the surface is formed by a highly cellular corium.

The vessels are everywhere dilated. The papillary and subpapillary channels are delicately widened and the interlobular passages show the same condition while in the non-epitheliomatous parts of the section the deep vessels are very conspicuous and here and there form great reservoirs like those seen in cavernous angiomata. These veins do not exhibit dilatation simply, for their walls are manifestly hypertrophic.

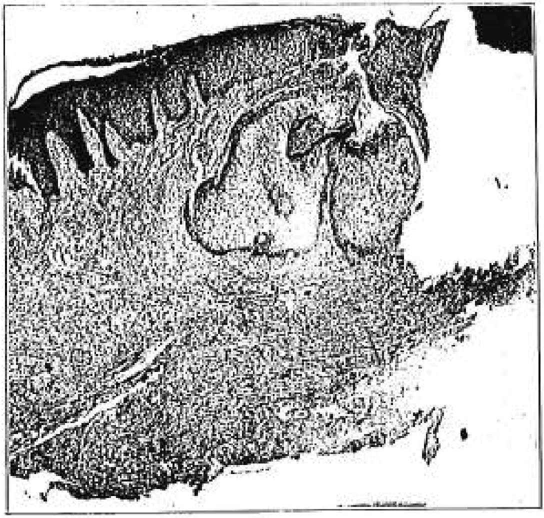
Curiously enough, pigmentation, which we associate so strongly clinically with X-ray dermatoses, seems to play no rôle throughout all these sections and hæmatin or melanin granules are conspicuously absent.

6. Ulcer: Tip of Third Finger of Right Hand.—This area presents a central ulceration with comparatively normal epidermis on each side. The floor of the ulcer is composed of string-like serpentine masses of epithelioid cells, groups of erythrocytes, polynuclear leucocytes and rather inconspicuous bundles of collagen. Lower down the field becomes less troubled. The pus cells and red corpuscles disappear. The epithelioid masses grow less numerous while mononuclear elements and connective tissue cells replace them. The epithelioid elements for the most part form worm-like processes; but in places this configuration is lost, branches develop or irregular masses are produced. These figures are composed of cells exhibiting large, oval or round nuclei which contain many nucleoli and are surrounded by meagre protoplasm with no retaining envelop. Here and there are especially large cells which seem to be pushing their way through lymph spaces.

7. From a Finger.—Here the epitheliomatous process is young. The epidermis shows a loss of the stratum corneum. The granular layer is practically wanting save for an occasional attenuated cell with but few granules. The upper layers of the rete are elongated and more or less devoid of nuclei. The germinal cells on the other hand are conspicuously numerous, absorb the stains deeply but show an irregular demarcation from the subjacent corium and exhibit occasional downward buds.

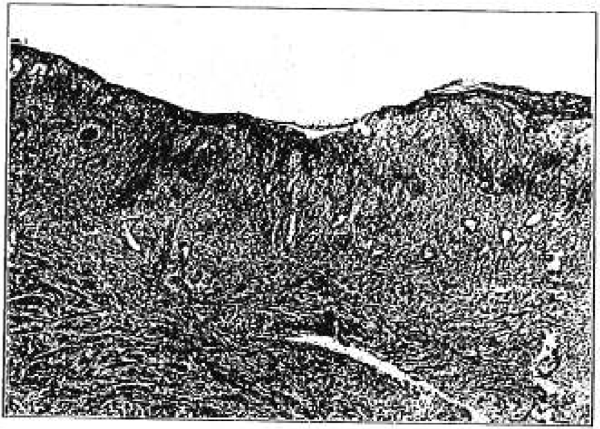
The corium presents dilated subpapillary vessels with hypertrophied endothelial cells while the deep veins are enormously enlarged with frequent great thickening of their several coats. In the sub-papillary layer there are striking masses of plasma cells with infrequent mast cells

FIG. 14.



Section from periphery of ulcer on back of right wrist, December, 1903.

FIG. 15.



Section from base of ulcer on back of right wrist, December, 1903.

especially about the vessels. Here again can be seen delicate string-like masses of epithelioid cells which wind through the lymph spaces. Where these masses widen out their component cells display large swollen nuclei. Evidences of chromatophores or of free pigment granules are once more wanting.

Where epitheliomatous changes are absent the connective tissue nuclei are appreciably elongated and enlarged.

Thus far these sections date from the operations of July 17, 1902.

Back of right wrist December 23, 1903 (Fig. 14). The epidermic structures are normal with the exception of a slight tendency toward irregularity where the palisade layer and corium meet and here certain nuclei are surrounded by clear spaces while others have dropped out and are replaced by inflammatory cells.

The papillary vessels are dilated with hypertrophied endothelium. The corium is very dense and is filled with mononuclear cells not particularly grouped but generally distributed.

At the periphery of the section, however, where the section ends abruptly through ulceration (?) there are two lobules of epithelial cells. One suggests the epidermis irregularly cut (cross section?), the other contains œdematous cells, some without nuclei, others swollen with large vesicular nuclei, others containing granules of keratohyalin—in fact the whole picture is strongly reminiscent of the epidermic changes seen in molluscum contagiosum. The whole structure is surrounded by inflammatory tissue.

8. *Back of Right Wrist.* (December 23, 1903, Fig. 15.)—To one side of the ulcerated area shown in the photograph the epidermis is greatly modified. The palisade layer forms a straight but broken line owing to the disappearance of the papillæ. The cell nuclei are round or oval rather than elongated, show one or more sharply staining nuclei and are filled with chromatin granules. The intercellular spaces are irregular and often enlarged. The overlying layers of the rete are thickened and present swollen, œdematous, loosely opposed cells mostly free of nuclei and spines. The granular layer is represented by free kerato hyalin granules only, all other evidences of granular cells having disappeared. Lastly, the stratum corneum is composed of many dense lamellæ with numerous persistent nuclei. Thus the whole epidermis presents acanthosis and parakeratosis of pure type.

In the corium the absence of papillæ has already been alluded to while the subpapillary vessels are widely dilated and exhibit hypertrophic endothelial cells. Below, the collagen is comparatively normal save for occasional swollen bundles. Moderately numerous plasma cells and rare mast cells are present, sometimes grouped about a distended vessel. Finally, deep down in the corium appear prominent veins now enothelially now totally thickened.

The ulcerated portion (Fig. 15) presents a complex picture of masses of polynuclear leucocytes and red cells lying in a mediumly coarse reticulation with interspersed large dilated vessels filled with erythrocytes and coagulated fibrin and with occasional processes of epithelial cells with grossly vesicular nuclei growing in from the sides or persisting as remnants. Below these abnormal elements lies a floor of thickened, rather anuclear collagenous bundles.

9. *Base of First Finger of Right Hand.* (December 23, 1903, Fig. 16.)—This represents scar tissue of considerable thinness. The epidermis consists for the most part of parallel bands of dense nucleated corneous lamellæ with occasional layers of rather amorphous, homogeneous, quasi rete cells containing infrequent round or oval nuclei surrounded by empty spaces. The germinal layer is represented by horizontally lying cells with flattened nuclei.

Even here the epidermis shows an effort toward downward proliferation foretelling future epitheliomatous growth.

The corium shows an absence of papillæ. The subpapillary layer is not as compact as one would suppose and its meshes are strewn with plasma cells, as seen in the photograph (16). There are frequent epitheliomatous cell nests, some solid and normal, others presenting varying degrees of central degeneration. In one (lying nearly centrally in the illustration) there is an outer ring of fair-sized, numerous, darkly-staining nuclei separated by a clear zone (artefact?) from the inner lamellated, flatly-nucleated layers which in their turn envelop an almost homogeneously degenerated centre containing an occasional giant nucleus and scattered nuclear debris and two large cysts partly filled with granulated protoplasm and mononuclear leucocytes.

The base is composed of practically normal fibrous tissue and the deep vessels when present exhibit no marked changes.

10. *Middle Finger of Left Hand.* (December 23, 1903.)—The tissue here is composed of a dense mass of fibrous elements devoid of all epithelial structures and free from vessels. It consists of practically structureless collagen on which lie small, round, solid-staining nuclei, the exact nature of which it is difficult to discern. In the deeper portion of the section the fibrous bundles form a reticulated mesh devoid of nuclei. The whole picture presents an extraordinarily blank mass.

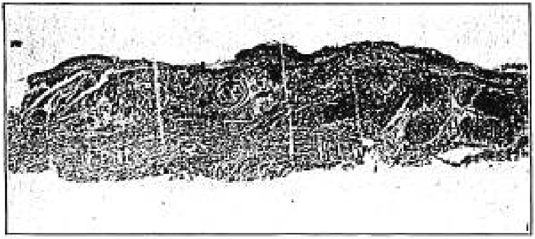
11. *Base of Third Finger of Right Hand.* (December 23, 1903, Fig. 17.)—The photomicrograph, 17, illustrates well the conditions present.

To one side an ulcerated surface of thickened collagenous material supporting numerous, many sized, mononucleated cells and small and large interstices containing erythrocytes with occasional whorls of œdematous and degenerated epithelial cells.

Where the epidermic covering is present the various layers are much altered. The rete shows an irregular base with marked tendency toward downward proliferation. The upper strata are emphatically hypertrophied while their component cells have lost their prickles and tend to coalesce, so that cell boundaries are gone, nuclei are swollen or absent and protoplasm is cloudy. The granular layer is represented for the most part by free kerato-hyalin granules. The stratum corneum is hyperplastic and nucleated. Again a marked picture of acanthosis and parakeratosis. Pigment is conspicuous by its absence.

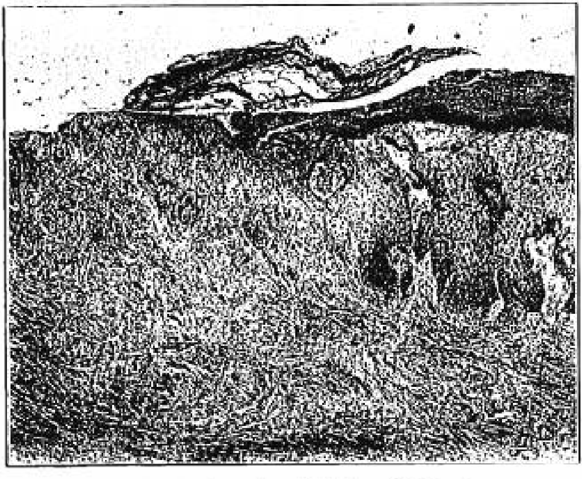
The corium exhibits only occasional papillæ which are filled with

FIG. 16.



Section from scar at base of first finger of right hand, December, 1903.

FIG. 17.



Section from tissue at base of third finger of right hand.

highly dilated vessels. The skeleton of the skin is composed of dense, rather anuclear bundles. Deeper vessels when present, show considerable thickening of their walls and constriction of their lumen and are surrounded by plasma and other mononuclear cells.

12. *Base of Little Finger of Left Hand.* (December 23, 1903.)—The process represented here is one of hyperkeratosis. The corium is dense. Vessels are slightly dilated and encompassed by extravasated mononucleated cells. Papillæ are insignificant. The rete is somewhat thickened for this part of the body but otherwise normal. The granular layer is manifestly hyperplastic and consists of five to six rows of large swollen cells with somewhat blunted ends and filled with masses of kerato-hyalin granules. The stratum lucidum is suggested but shows no traces of eleidin. The stratum corneum is conspicuously thickened and composed of layer upon layer of waving horny cells.

13. *Tip of Middle Finger.* (September 19, 1904.)—A very complex and irregular picture. The epidermis is mostly gone, the few surviving vestiges being quite atypical. The corium is totally abnormal and it is difficult to orientate oneself.

The upper layers are filled with dense masses of plasma cells and with sparsely scattered lymphocytes. Small dilated vessels with extraordinarily vesicular nuclei abound choked with red cells and occasional lymphocytes. The supporting fibrous tissue is in places dense, in others delicately reticulated, the intensity of the plasmomata corresponding directly with the density of the collagen. Here and there are small lobules of epithelial cells, occasionally whorls and more rarely branching tubules. All three forms exhibit absence of prickles and presence of highly vesicular cells containing one or two nucleoli and dense chromatin granules. The whorls and the tubules show a tendency toward central hyalin degeneration. When visible through comparative freedom from inflammatory invasions, the fibrous tissue shows a moderate proliferation of its nuclei.

14. *Base of Middle Finger.* (September 19, 1904.)—Great hyperplasia of the rete is the distinguishing feature here. For the most part the change is purely one of overgrowth in the depth of the layer. The cells are normal although somewhat œdematous and there is marked intercellular invasion of leucocytes. Here and there, however, the cellular elements show loss of prickles, vacuolization and tendency towards homogeneity. The stratum granulosum is represented mostly by free lying kerato-hyalin granules with occasional areas of partly developed granular cells. The horny layer is compact but otherwise normal.

The dividing line between epidermis and corium is so indefinite owing to the great overgrowth of the rete and the irregularity of the cut that it is difficult to ascertain the presence or absence of papillæ. There are numerous foci of snared-off epithelial clusters. The corium is dense and interspersed with numerous plasma cells, especially in the subpapillary layer.

15. *Keratosis from Dorsal Base of Middle Finger of Right Hand.*—This region presents an epidermic picture somewhat similar to the last

but here one finds the additional presence of a hyperplastic horny layer containing some nuclear cells. Again, the demarcation between corium and epidermis is well marked and the palisade layer more normal. Papillæ are present and hold dilated vessels—in one instance the whole papillary space is occupied by a vessel whose wide lumen is partially filled with lymphocytes, polynuclear leucocytes, erythrocytes and granular or reticulated fibrin. The corium presents the condition so frequently described in these sections, *i.e.*, dense collagen with dilated vessels and extravasated mononuclear cells.

16. *Tip of Little Finger.* (September 19, 1904.)—Another picture of parakeratosis and acanthosis with absence of papillæ and dense infiltrated corium.

17. *Ulcer on Back of Left Hand.* (October 16, 1904).—A complicated structure. The epidermis is entirely gone and the corium contains many polymorphous epithelial lobules and whorls; superficial dilated vessels blocked with red and with white cells; and innumerable endothelial and mono- and polynuclear elements. The epithelial whorls and lobules consist in the majority of instances of spine-bearing cells and present all stages of degeneration even to cystic spaces containing chromatin granules and reticulated or granular protoplasmatic debris.

The underlying corium is composed of dense fibres with elongated and enlarged nuclei and the deeper vessels are murally thickened.

18. *Keratosis of Right Wrist.* (October 16, 1904.)—Once more conditions now so familiar in this series of sections. Here one finds a hyperplastic rete whose upper layers are œdematous and degenerated; a total absence of granular cells and even independent granules; and an enormously overgrown horny layer bearing nucleated scales and leucocytic crusts.

Papillæ are insignificant. Subpapillary vessels slightly dilated. Collagen delicate in structure and supporting some mononuclear extravasated cells.

Sections from five other excised portions of this same date show pictures presenting the various characteristics which have marked those previously described and need not be detailed again.

19. *Graft Upon Middle Finger of Left Hand.* (October 16, 1904.)—The artificial epidermic covering is to all intents and purposes normal, but in one portion of the section the insidious process has redeveloped and below the rete one finds the now familiar epithelial lobules with central hyaline degeneration.

20. *Keratosis from Forehead.* (December 27, 1904.)—A newly invaded field. This section illustrates almost perfectly the epidermic characteristics of the sole of the normal foot. The rete is somewhat thickened, the cells of the upper transitional layers more or less vesicular and thrown up into jagged summits and depressions into which dovetail layer upon layer of normal horny cells. The corium, however, shows evidences of considerable inflammation. Vessels are dilated and plasmomata are frequent. Sweat and sebaceous glands hitherto not observed in these sections are present in great abundance and exhibit no marked deviation from the normal.

21. *Forehead.* (April 20, 1905.)—The intervening five months have wrought a great change. In the present section ulceration has occured and at the epithelial edge the cells of the upper layers of the rete are flattened and contain peri-nuclear halos or empty nuclear spaces; all semblance of granular cells has vanished; and a thin, parakeratotic horny layer is present. The lower layers of the rete are running riot. They have overcome the normal resistance of the corium and are proliferating enormously into the subjacent structures. Individual cells are often of enormous size and have become amorphous, anuclear swollen masses of protoplasm. In other areas large vesicular nuclei are present with but scant surrounding protoplasm. Cellular invasion is absent.

Farther down in the corium hugely swollen, anuclear bundles of collagen and some veins of extraordinary thickness and jagged, slit-like lumen appear. These unusual collagenous fibres would suggest an incipient colloid degeneration. The sweat glands remain strangely unaffected in the midst of these contiguous pathological structures.

22. *Hand.* (November 8, 1905.)—These sections are cut largely in so horizontal a plane that it would be injudicious to judge of the epithelial changes. There is, nevertheless, marked hyperplasia of the rete with occasional loss of nuclei especially in the germinate zone, general cloudiness of the cells and some intercellular leucocytic invasion. In places all vestiges of normal metamorphosis from rete to horn cells have gone and the free surface of the skin forms a chaotic mass.

The subpapillary layers, which alone are present, show fine reticulation supporting normal vessels and a general plasmomatic infiltration.

23. *Keratosis from the Hand.* (November 8, 1905.)—Here one has an ideal representation of a papillary and verrucous nævus. The rete is cast in individual rounded lobes formed by the fine and widely separated ascending papillæ and in places these lobes strongly suggest the lower rete conformation of molluscum contagiosum. In these lobes the rete is hyperplastic and fairly normal although perinuclear halos are common. The granular cells also exist in great numbers and one can count ten to twelve perfectly developed layers while above, before keratinization has been completed, as many more layers, half granular, half keratinous, appear. Above these increased strata lie row upon row of typical horn cells. Thus far the description has related to the interpapillary lobes but as is the rule in nævous pictures the rete and granular layers surmounting the papillæ do not present these hyperplasias but appear in comparatively normal amounts.

The papillæ are proportionately narrow but project far into the epidermis, in some instances to extraordinary distances. As is customary in this class of nævi the papillary and subpapillary vessels are slightly dilated and accompanied by a moderate number of mononucleated cells which lie between and under the epidermic lobes. The rete is practically normal.

24. *Ulnar Side of Forefinger.* (November 8, 1905.)—A mild degree of the preceding process, partly purely keratotic and partly slightly papillomatous.

25. *Ulceration of Finger.* (November 8, 1905.)—An intensely interesting picture of multiform and generalized degeneration which has affected practically all the various structures of the skin.

The epidermis is represented by remnants of previous downshoots from the rete which persist as barely recognizable, swollen, amorphous, acid staining protoplasm with occasional vesicular nuclei.

The papillæ of the corium are gone and the subpapillary layer holds numerous moderately dilated vessels within frequent, cloudy vesicular endothelial cells and with swollen lymphocytes, a few pus cells and reticulated fibrin in their channels. Collagen appears as straight, œdematous bundles between which extend chains of oblong plasma cells and more irregularly distributed lymphocytes. These plasma cells are histologically noteworthy for one seldom sees such well defined examples with their eccentrically placed, round nuclei bearing symmetrically arranged peripheral nucleoli.

These rows of alternating plasma cells and swollen collagen are interrupted by frequent vessels whose walls are cloudy and whose nuclei are vesicular and often of great size. Below, there are isolated or grouped masses of wavy or serpentine basic-staining elastic fibres (elacin) which lie between the fibrous bundles or form large, solid areas free from collagen.

26. *Outer Side of Forefinger.* (November 8, 1905.)—Another ulcerated surface disclosing many of the attributes of the previous section but not containing so many interesting histological features.

27. *Back of Right Hand.* (March 16, 1906.)—In this section there are stretches of epidermis and of ulceration. Where the former is present there is some tendency toward hyperplasia of the rete while the stratum granulosum is absent and the stratum corneum is represented by a thin homogeneous mass. Underneath, the corium is normal except for universally dilated vessels surrounded by plasmomata.

Where the epidermis is gone the corium is filled with circular or polymorphous lobules of epithelial cells which show no tendency toward degeneration. Multiple dilated vessels with lumens choked with red cells lie between these epitheliomatous masses and scattered universally throughout the depth of the derma are many mono- or polynucleated inflammatory cells.

28. *First Finger of Left Hand.* (March 16, 1906.)—A pathological condition similar to the last but here the epidermis is intact, exhibiting hyperplasia of the rete and of the horny layer, both of which are infiltrated with many leucocytes usually of the pustular type. Here also evidences of downward proliferation of the rete are visible. Finally there is abundant hæmorrhage everywhere.

29. *Tip of Third Finger.* (March 16, 1906.)—This piece of skin is free from epitheliomatous changes. For long stretches the upper layers of the epidermis are wanting while the corium exhibits in all parts many dilated vessels and multitudinous plasma cells.

30. *Excision.* (November 4, 1906.)—This section, the last in this long series, exhibits undiminished evidences of epithelioma.

The horny layer is practically non-existent, the granular layer is normal. The rete is in places thickened and displays numerous infiltrating leucocytes and at its germinate layer evinces signs of downward-penetrating proclivities. Papillæ are present and bear slightly dilated vessels. The subpapillary layer is delicately reticulated and holds frequent plasmomata and distended vessels containing fibrous meshes and occasional polynuclear leucocytes. Just below this level lies another series of plasma cell masses whose characteristics are strikingly visible and immediately subjacent are extensive areas of epithelial whorls and lobules surrounded by still further plasma cells.

The outer lamellations of these whorls show well differentiated prickle-bearing cells; but within lie degenerated, puffed cells, free from prickles and at times from cell boundaries, containing frequently giant nuclei or no nuclei at all and more mitotic figures than in the previous pathological history of the case. Finally, in the very centre of some of the whorls are found large cysts partially filled with coagulated fibrin, giant nuclei and abundant chromatic remains. Where these cysts appear the epithelial masses are more "pearly" than elsewhere.

This, then, is the detailed description of the pathological side of this discouraging history, and it is distressing to find at the end of this long series a slide exhibiting the most active phases of the disease.

One who has read the histological minutiæ of the case will be struck, presumably, by the manifold varieties of the pathological structures. Almost every known phase of epidermic deviation has been encountered, and the cellular, vascular, and protoplasmic alterations and degenerations have been most varied and interesting. The one striking omission in the case has been the unexpected absence of all pigmentary signs, especially when one remembers how prominent a clinical feature pigmentation is in X-ray dermatitis and its epitheliomatous sequelæ.